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Docket No. MCP-262

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Bunick, et al.
Serial No.	:	09/752,899
Filed	:	December 29, 2000
Title	:	SOFT TABLET CONTAINING DEXTROSE MONOHYDRATE
Art Unit	:	1615
Examiner	:	C.L. Evans

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August 4, 2004
(Date of Deposit)

Timothy E. Tracy
(Name of applicant, assignee, or Registered Representative)


(Signature)

August 4, 2004
(Date of Signature)

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APPEAL BRIEF

Dear Sir:

In accordance with the provisions of 37 CFR § 1.191, a timely Notice of Appeal was filed in the captioned application on April 12, 2004. A petition for a two-month Extension of Time is submitted concurrently herewith. Accordingly, this Appeal Brief is timely filed, with an executed Certificate of Mailing on or before August 12, 2004. Three copies of the Appeal Brief are enclosed.

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1) Real Party in Interest

The real party in interest in the application in this appeal is Applicants' assignee McNeil-PPC, Inc., a corporation of New Jersey, a wholly owned subsidiary of Johnson & Johnson, a New Jersey corporation.

(2) Related Appeals and Interferences

No related appeals or interferences are known to exist.

(3) Status of the Claims

Claims 1-5 and 7-13 are the claims on appeal, a copy of which are attached hereto in the Appendix to this Brief. Claim 6 has been cancelled. No claims stand allowed in this application.

(4) Status of Amendments

The Amendment submitted in Paper No. 10 was entered in the captioned application according to Paper No. 11, dated June 12, 2003.

(5) Summary of the Invention

The present invention provides a tablet capable of being chewed or disintegrated in the oral cavity prior to swallowing, containing a pharmaceutically active ingredient and a matrix comprising directly compressible dextrose monohydrate and about 0.005 to about 10 % by weight of sucralose. The tablet contains less than 5% by weight of fat and said matrix is substantially free of non-saccharide, water soluble polymeric binders.

(6) Issues on Appeal

(A) Whether the inventions of claims 1-5 and 7-13 are unpatentable under 35 USC § 103(a) over Valentine (U.S. Pat. No. 4,684,534) ("Valentine") in view of Puglia et al. (U.S. Pat. No. 4,327,076) ("Puglia").

(7) Grouping of Claims

It is believed that all of the pending claims are patentable over the rejection made by the Examiner. For purposes of this Appeal, claims 1-5 and 7-13 stand and fall together.

(8) Argument

(iv) Rejection under 35 USC § 103

Claims 1-5 and 7-13 were rejected as being unpatentable under 35 USC § 103(a) over Valentine in view of Puglia. (Paper No. 13 at 4.)

For the reasons set forth below the rejection, respectfully is traversed.

Valentine discloses

> and contacted by the liquid. The tablet has particular utility as a chewable tablet which resists absorption of moisture but which quickly liquifies and melts in the mouth within seconds after mastication, even if the tablet contains considerable amounts of active ingredients that do not dissolve well or at all in the mouth. Also disclosed are agglomerates from which the tablets are directly compressed, and processes for making the agglomerates and tablets. The tablets contain increased quantities of active ingredients of up to about 75% by weight. The excipient or base material of the tablet is made from carbohydrates including dextrose, dextrose monohydrate, maltodextrin, fructose, sucrose, lactose, maltose and xylose held together by small quantities of a carbohydrate binder such as maltodextrin. Tablets according to the invention can contain active ingredients such a pharmaceuticals (e.g., antacids, analgesics, cough medicine, drugs, etc.) breath sweeteners, vitamins and dietary supplements, to name a few.

Abstract

> forms.
>
> The carbohydrate-based agglomerates comprise carbohydrate particles selected from the group consisting of dextrose, dextrose monohydrate, maltodextrine, fructose, sucrose, lactose, maltose and xylose; and a water-soluble binder selected from the group consisting of maltodextrine, corn syrup solids, dextrose, sucrose, polyvinylpyrollidone and cooked starch paste. The quantity of water-soluble binder is somewhat critical and should be in the range of from about 1 percent to about 10 percent by weight of the agglomerate (without active ingredient), and preferably from about 1 percent to about 5 percent, with the carbohydrate-based particles comprising from about 90 percent to about 99 percent by weight of the agglomerate (without active ingredient). The particle size of the materials used to make the agglomerates and the tablet have been found to be important, as described below.

Col. 2.

> dient). The agglomerate and entrained active ingredient have particular utility as a direct compression agglomerate from which tablets according to the invention can be made, particularly chewable tablets which liquify in saliva.

Col. 3.

A process for making the carbohydrate-based agglomerate comprises the steps of forming a fluidized bed of the carbohydrate particles, intermittently spraying a solution of the water soluble binder in a droplet size of from about 20 microns to about 100 microns into the fluidized bed so as to cause intimate comingling of solution and carbohydrate particles and adhesion together of carbohydrate particles to form agglomerated particles, drying the particles in the fluidized bed between intermittent sprayings, and continuing spraying and drying until the desired amount of solution has been sprayed into the bed. Thereafter, the agglomerated particles are dried to a desired moisture content or the equilibrium moisture content. The amount of liquid binder solution sprayed corresponds to a binder content in the agglomerate of from about 1 percent to about 10

Col. 3

percent by weight of the agglomerate (excluding active ingredient). The carbohydrate-based agglomerate, and an active ingredient are mixed, preferably in a low shear blender, in the following proportion by weight of the finished agglomerate (including active ingredient):agglomerate, about 50 percent to about 90 percent; active ingredient, from about 10 percent to about 50 percent. A lubricant is also mixed together with the agglomerate and the active ingredient in the proportion of from about 0.4 percent to about 1 percent by weight of the finished agglomerate (including active ingredient). Flavors can also be mixed with the agglomerate and active ingredient.

Col. 4.

The agglomerate can, as formed, entrain the active ingredient and other materials such as a lubricant and flavors. In addition, an agglomerate including the en-

Col. 4

The carbohydrate particles passed 50 mesh (particle size less than about 300 microns), and the water-insoluble active ingredients passed 325 mesh (particle size less than about 44 microns). Lubricant particles passed 325 mesh and other materials such as flavors passed 100 mesh. The precise size of the carbohydrate particles is not critical, but agglomerates made from materials having sizes larger than about 50 mesh for the carbohydrate particles and larger than about 300 mesh for the active ingredient do not produce tablets which liquify and melt in the mouth as quickly and as completely as those made with smaller particles. Active ingredients which do not dissolve in the liquid in which a tablet made from the agglomerate is to liquify, e.g., water or saliva, preferably have a particle size of less than about 10 microns. A preferred particle size for such active ingredients is from about 3 microns to about 10 microns. Before being compressed into tablets, the agglomerate particles are sized −22 mesh, +100 mesh (between about 150 microns and about 800 microns). The agglomerate particle size is also not critical and particles in the above range produce tablets having preferred characteristics.

Col. 9

EXAMPLE XIII

In Example XIII, a direct compression agglomerate including an active ingredient was processed directly, as generally described for Example I. The process parameters were as follows:

Atomizing air pressure	4 atm
Pattern air pressure	4 atm
Atomizing air flow rate	170 M^3/hr
Pattern air flow rate	20 M^3/hr
Liquid binder flow rate	30 ml/min.
Fluidizing air temperature	30° C.
Binder solution	10 liters of 10% w/w maltodextrin in water

The particles were dried to a moisture content of 4.0% and screened −22 mesh, +88 mesh.

In XIII A–C below, the charge was 60 kg and in XVII D and E, the charge was 300 gm. In XIII A–D, the flavors, the citric acid and the magnesium stearate, were added after the agglomerate was formed. The particle size of the calcium carbonate was about 3 microns to about 10 microns. The magnesium stearate passed −325 mesh and the flavors passed −100 mesh.

	A % w/w	B % w/w	C % w/w	D % w/w	E % w/w
Calcium Carbonate	25.00	49.00	40.00	76.6	52.00
Dextrose (−50 mesh)	71.25	48.50	57.00	22.2	43.90
Maltodextrin	2.54	1.29	2.79	—	1.09
Maltodextrin as 10% Aqueous Solution	1.21	1.21	1.21	2.2	1.21
Flavors	0.20	0.20	0.20	0.20	0.36
Citric Acid	1.00	1.00	1.00	1.00	1.00
Magnesium Stearate	0.60	0.60	0.60	0.60	0.50

The agglomerates of Example XIII were observed to have generally the characteristics of the agglomerates of Examples I–XII except that they entrained up to about 76.6% by weight of an active ingredient.

Col. 13.

Puglia discloses

An improved compressed soft chewable tablet is provided, which may contain an antacid or other active ingredient, has good flexibility, is breakage resistant and disintegrates immediately upon chewing. The tablet of the invention is formed of particles of a recrystallized fatty material, such as chocolate, a bulking material such as sugar or an active ingredient, such as an antacid, bound up in the particles of recrystallized fatty material, and a direct compaction vehicle which binds the particles of recrystallized fatty material and bulking material, under compression, into a chewable tablet.

Abstract

In accordance with the present invention, a unique compressed chewable tablet is provided which has excellent hardness and flexibility, is breakage and chip resistant and yet may be easily chewed and quickly disintegrated and dissolved in the mouth. The compressed chewable tablet of the invention includes a particulate recrystallized fatty material having a bulking material or agent bound up therein and a direct composition vehicle which binds the combined particles of recrystallized fatty material and bulking material, under compression, into a chewable tablet. Col. 2

The fatty material employed herein will preferably be in the form of chocolate or a synthetic chocolate, such as compound coating or "Ice-Cap coating" (Nestle's synthetic chocolate formed of hydrogenated fat, emulsifier, flavor, sugar and milk solids). These fatty materials are preferred because they provide excellent flavor and sweetness with the requisite amounts of fats, (in the form of hydrogenated fats), that is, fats in an amount of from about 5 to about 20% and preferably from about 10 to about 14% by weight of the finished chewable tablet. Since the hydrogenated fats account for about 30 to about 40% of the chocolate or synthetic chocolate, the chocolate materials may be present in an amount of from about 20 to about 55% and preferably from about 35 to about 45% by weight of the finished compressed tablet. It has been found that where larger amounts of fats are employed, the fats must be pretreated and absorbed on a carrier, such as cornstarch, to facilitate compaction. In the present invention, no such pretreatment is required. Col. 3.

sium trisilicate.

Preferred antacids include aluminum hydroxide, calcium carbonate, magnesium carbonate and mixtures thereof as well as magnesium hydroxide.

Any emulsifier or surfactant approved for use in foods by the Food & Drug Administration and having an HLB value of 8 and above, may optionally be employed in the chewable tablets of the invention in amounts ranging from about 0.05 to about 2.5% by Col. 4

The antacid tablets as well as the other compressed tablets of the invention may also include one or more other pharmaceutically acceptable agents, as desired, such as sweetening agents, including sugars, sugar alcohols, hydrogenated starch hydrolysates (Lycasin) and synthetic sweeteners, such as sorbitol, xylitol, saccharin salts, free acid form of saccharin, cyclamate salts, free cyclamic acid, dihydrochalcones, L-aspartyl-L-phenylalanine methyl ester, isomaltitol (Palatinit), as well as coloring agents, other flavoring agents, disintegrating agents, such as starch, other binding agents, lubricants, such as calcium stearate, stearic acid, magnesium stearate (0.5 to 3% by weight), antioxidants, such as butylated hydroxy toluene, antiflatulents, such as simethicone, bulking agents such as polydextrose and the like. Col. 5

Ingredient	Parts by Weight of Tablet
Ice cap coating (Nestle) (fat, emulsifier, artificial flavor, sugar, milk solids)	40
Suntone 8-1-0 (emulsifier - polyglycerol ester of fatty acids, HLB 13)	0.5
Chocolate flavor	0.5
Confectioners sugar	31
Cantab (dextrose monohydrate)	28

Col. 7.

In making the rejection, the Examiner merely stated that "[t]he rejection is maintained." (Paper No. 13 at 4.) In the previous rejection, the Examiner asserted that Valentine "teaches a chewable tablet comprised of active ingredients such as antacids, analgesics, cough medicine and drugs." (Paper No. 11 at 3.) The Examiner contended that "[t]he chewable tablet also contains dextrose monohydrate and sucrose and that "sucrose is present from about 1% to about 10% binder by weight." (*Id.*) The Examiner further contended that Valentine "teaches" compressible dextrose monohydrate and that the referenced agglomerates were made from a liquid binder solution of materials and carbohydrate materials, which include materials such as dextrose monohydrate. (Paper No. 13 at 2.) The Examiner asserted that both sucrose and sucralose are sweeteners. (*Id.* at 3.) The Examiner acknowledged, however, that Valentine differs from the presently claimed invention in that Valentine

1. "does not expressly teach sucralose" (Paper No. 11 at 3);
2. is "silent regarding percent weight of water soluble polymeric binders" (*Id.* at 3);
3. desires smaller particle sizes (*Id.* at 4); and
4. "does not expressly teach fats" (*Id.* at 4).

To fill the acknowledged gaps, the Examiner relied upon

1. the fact that sucrose is the starting material for sucralose (*Id.* at 4);
2. More legal reasoning;
3. "the active ingredient can have particle sizes larger than about 50 microns (*Id.* at 4);

4. Puglia as "teaching a compressed chewable table comprised of fats employed in amounts within the range of about 2 to 45% (column 4, lines 61-63)" (*Id.* at 4).

The Examiner then concluded that

1) since sucrose is a starting material to make sucralose, "it would be an obvious variation to substitute sucrose for sucralose" (*Id.* at 3) and "the presence of the sucrose or sucralose is all the is needed to render obvious applicant's claim" (Paper No. 13 at 3.)

2) differences in concentration of the percent weight of polymeric binders will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating that such concentration is critical (Paper No. 11 at 2.)

3) Valentine's active ingredient particle size can be larger than about 50 microns and one having ordinary skill in the art would have been expected to determine the optimum particle size during routine experimentation (*Id.* at 4); and

4) "[i]t would have been prima facie obvious to one of ordinary skill in the art at the time of th einvention to use the teachings of Puglia into the teachings of Valentine because Puglia teaches that employing fats into the chewable tablet compositions would provide the expected result of improved taste." (*Id.*)

Obviousness, cannot be based upon speculation. Nor can obviousness be based upon possibilities or probabilities. Obviousness ***must*** be based upon facts, "cold hard facts." When a conclusion of obviousness is not based upon facts, it cannot stand.

"Determination of obviousness cannot be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention." ATD Corp. v. Lydall, Inc., 159 F.3d 534, 546, 48 USPQ2d 1321, 1329 (Fed. Cir. 1998). There must be a teaching or suggestion within the prior art, within the nature of the problem to be solved, or within the general knowledge of a person of ordinary skill in the field of the invention, to look to particular sources, to select particular elements, and to combine them as combined by the inventor. See Ruiz v. A.B. Chance Co., 234 F.3d 654, 665, 57 USPQ2d 1161, 1167 (Fed. Cir. 2000); ATD Corp, 159 F.3d at 546, 48 USPQ2d at 1329; Heidelberger Druckmaschinen AG v. Hantscho Commercial Prods., Inc., 21 F.3d 1068, 1072, 30 USPQ2d 1377, 1379 (Fed. Cir. 1994) ("When the patented

invention is made by combining known components to achieve a new system, the prior art must provide a suggestion or motivation to make such a combination.").

VALENTINE DOES NOTAPPEAR TO DISCLOSE AS MUCH AS THE EXAMINER ASSERTED

The Examiner asserted that "[t]he chewable tablet also contains dextrose monohydrate and sucrose." However, it is not seen where such disclosure is made in Valentine.

Valentine's abstract discloses that "[t]he excipient or base material of the tablet is made from carbohydrates including ... dextrose monohydrate, ... sucrose, and xylose." Valentine further discloses that [t]he carbohydrate-based agglomerates comprise carbohydrate particles **selected from the group consisting of** dextrose monohydrate, ... sucrose, ... **and** xylose." (emphasis added.) (Col. 2, lns. 30-33.) Similar disclosure is found in claims 3, 15, 23, 30, 40, 47, and 50.

It is not seen where the above disclosure supports the proposition of a tablet having **both dextrose monohydrate and sucrose**. In fact, the words "and mixtures thereof" or "combinations thereof" and the like do NOT appear to be used by Valentine when describing the list of possible carbohydrates. Except for maltodextrin, which is explicitly listed as a carbohydrate and a binder, it is not seen where Valentine intended to suggest that mixtures of the listed carbohydrates could be used in the disclosed invention. This proposition is further supported by the Examples in Valentine. Nor is it seen where Puglia provides support for the Examiner's position. Because Valentine alone or in combination with Puglia appear to not to disclose as much as the Examiner contended, the rejection is improper and should be withdrawn.

The Examiner also concluded that "the active ingredient can have particle sizes larger than about 50 microns." However, it is not believed that this proposition is valid for the entire universe of carbohydrates and active ingredients. Valentine expressly discloses that tablets having carbohydrates and water insoluble active ingredients particle sizes greater than 300 microns and 50 microns, respectively, liquefy too slowly in the mouth." (*See*, col. 4, lns. 29-46.) It is not seen where Puglia closes the gap left by Valentine. For this additional reason, the rejection cannot stand and should be withdrawn.

PUGLIA DOES NOT APPEAR TO DISCLOSE AS MUCH AS THE EXAMINER ASSERTED

The Examiner asserted that "Puglia teaches a compressed chewable tablet comprised of fats employed in amounts with the range of from about 2 to 45% (column 4, lines 61-63)." However, review of column 4, lines 61-63 of Puglia indicates that preferred antacids are disclosed therein, not fats, much less a disclosure of any amount of fats. It is not seen where the Examiner obtained the quoted fat levels from, but it cannot be located based on the information provided by the Examiner. For this additional reason, the rejection is improper and should be withdrawn.

Nonetheless, it has been located in Puglia at column 3, lines 11-17, that fats can be in an amount of from about 5 to about 20% by weight of the finished chewable tablet. Currently pending claims 1-11 are directed to, among other things, a tablet containing less than 5% by weight of fat and currently pending claims 12-13 are directed to, among other things, a tablet being substantially free of triglycerides. It is not seen where the current record provides any motivation or support for a tablet having, among other things, the claimed fat and triglyceride levels. For this additional reason, the rejection is improper and should be withdrawn.

Record Does Not Support Mere Substitution of Sucralose for Sucrose

In making the rejection, the Examiner relied on the fact that a because sucrose is starting material to make sucralose and they are both sweeteners, to conclude that it would be "an obvious variation to substitute sucrose for sucralose."

The Examiner used the incorrect standard for concluding that substitutability of sucrose for sucralose. Merely stating it would be "an obvious variation" does not satisfy the strict requirements to make a proper prima facie case of obviousness. The Examiner has not satisfied the legal mandate for making such a rejection. For this additional reason, the rejection is improper and should be withdrawn.

The section of the document relied on by the Examiner "to demonstrate the interchangeability of the sucrose and sucralose, Liu (WO 99/47126, page 13, line 15), merely discloses "the SPLENDA® Brand Sweetener). Sucralose is a chlorinated sucrose derivative,." The remainder of the paragraph discloses various physical and chemical characteristics of sucralose. However, it is not seen where the line in Lui cited by the

Examiner supports the proposition advocated by the Examiner. For this reason, the record does not support the rejection and it should be withdrawn.

Accordingly, for the reasons set forth above, withdrawal of the rejection, and allowance of the claims is respectfully solicited

Respectfully submitted,

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APPENDIX

(9) Claims on Appeal

Claim 1 (previously presented): A tablet capable of being chewed or disintegrated in the oral cavity prior to swallowing, comprising a pharmaceutically active ingredient, and a matrix comprising directly compressible dextrose monohydrate and about 0.005 to about 10 % by weight of sucralose, said tablet containing less than 5% by weight of fat and said matrix being substantially free of non-saccharide, water soluble polymeric binders.

Claim 2 (original): The tablet of claim 1, wherein the active ingredient is selected from the group consisting of acetaminophen, ibuprofen, pseudoephedrine, dextromethorphan, diphenhydramine, chlorpheniramine, calcium carbonate, magnesium hydroxide, magnesium carbonate, magnesium oxide, aluminum hydroxide, mixtures thereof, and pharmaceutically acceptable salts thereof.

Claim 3 (original): The tablet of claim 1, wherein the directly compressible dextrose monohydrate has an average particle size of about 100 to about 250 microns.

Claim 4 (original): The tablet of claim 1, wherein the weight ratio of dextrose monohydrate to sucralose is at least about 25:1.

Claim 5 (original): The tablet of claim 1 containing about 15 to about 90 % by weight of dextrose monohydrate based on the total weight of the tablet.

Claim 6 (cancelled)

Claim 7 (original): The tablet of claim 1 containing less than 3 % by weight fat.

Claim 8 (original): The tablet of claim 1 being substantially free of aspartame.

Claim 9 (original): The tablet of claim 1 wherein the pharmaceutically active ingredient has an average particle size from about 100 to about 500 microns.

Claim 10 (original): The tablet of claim 1 manufactured by a direct compression or dry granulation process.

Claim 11 (original): The tablet of claim 1 being substantially free of microcrystalline cellulose.

Claim 12 (previously presented): A tablet capable of being chewed or disintegrated in the oral cavity prior to swallowing, comprising a pharmaceutically active ingredient; and a matrix comprising directly compressible dextrose monohydrate; about 0.005 to about 10 % by weight of sucralose; at least one disintegrating agent selected from microcrystalline cellulose, starch, sodium starch glycolate, crosslinked polyvinylpyrrolidone, crosslinked carboxymethylcellulose, and mixtures thereof; at least one lubricant selected from magnesium stearate, stearic acid, and mixtures thereof; and optionally an auxiliary ingredient selected from fillers, sweeteners, surfactants, glidants, acidulents, antioxidants, preservatives, coloring, flavoring agents, and mixtures thereof; said tablet being substantially free of triglycerides and said matrix being substantially free of non-saccharide, water soluble polymeric binders.

Claim 13 (previously presented): The tablet of claim 12 wherein the tablet comprises no more than 25 % by weight of said optional auxiliary ingredients.